EXHIBIT

1

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BLink, Conserved Domains, Links

1: 721P. Reports Chain , H-Ras P2...[gi:494925]

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LOCUS       721P                    166 aa            linear   PRI 07-OCT-1998
DEFINITION  H-Ras P21 Protein Mutant With Gln 61 Replaced By Leu (Q61L) Complex
            With Guanosine-5'-[b,G-Imido] Triphosphate.
ACCESSION   721P
VERSION     721P  GI:494925
DBSOURCE    pdb: molecule 721P, chain 32, release Jun 6, 1991;
            deposition: Jun 6, 1991;
            class: Oncogene Protein;
            source: Human (Homo Sapiens) Cellular Harvey-Ras Gene Truncated And
            Expressed In (Escherichia Coli);
            Exp. method: X-Ray Diffraction.
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 166)
  AUTHORS   Pai,E.F., Krengel,U., Petsko,G.A., Goody,R.S., Kabsch,W. and
            Wittinghofer,A.
  TITLE     Refined crystal structure of the triphosphate conformation of H-ras
            p21 at 1.35 A resolution: implications for the mechanism of GTP
            hydrolysis
  JOURNAL   EMBO J. 9 (8), 2351-2359 (1990)
   PUBMED   2196171
REFERENCE   2  (residues 1 to 166)
  AUTHORS   Krengel,U., Schlichting,L., Scherer,A., Schumann,R., Frech,M.,
            John,J., Kabsch,W., Pai,E.F. and Wittinghofer,A.
  TITLE     Three-dimensional structures of H-ras p21 mutants: molecular basis
            for their inability to function as signal switch molecules
  JOURNAL   Cell 62 (3), 539-548 (1990)
   PUBMED   2199064
REFERENCE   3  (residues 1 to 166)
  AUTHORS   Krengel,U., Scherer,A., Kabsch,W., Wittinghofer,A. and Pai,E.F.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JUN-1991)
COMMENT     Revision History:
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Mutant according to the invention!
P. 52/l. 24

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Range: from begin to end Reverse complemented strand Features: SNP graph CDD MGC HPRD STS tRNA
1: AB006590. Reports Homo sapiens mRNA...[gi:2911151] Links

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ACCESSION   AB006590
VERSION     AB006590.1  GI:2911151
KEYWORDS    estrogen receptor beta.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Ogawa,S., Inoue,S., Watanabe,T., Hiroi,H., Orimo,A., Hosoi,T.,
            Ouchi,Y. and Muramatsu,M.
  TITLE     The complete primary structure of human estrogen receptor beta (hER
            beta) and its heterodimerization with ER alpha in vivo and in vitro
  JOURNAL   Biochem. Biophys. Res. Commun. 243 (1), 122-126 (1998)
   PUBMED   9473491
REFERENCE   2  (bases 1 to 1740)
  AUTHORS   Ogawa,S.
  TITLE     Direct Submission
  JOURNAL   Submitted (13-AUG-1997) Sumito Ogawa, Saitama Medical School,
            Department of 2nd Biochemistry; 38 Morohongo, Moroyama, Iruma-gun,
            Saitama 350-0495, Japan (E-mail:suogawa@saitama-med.ac.jp,
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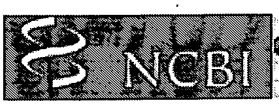

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Range: from begin to end Features: SNP graph CDD MGC HPRD STS tRNA Refre

1: 1204262A. Reports estrogen receptor...[gi:224957]

BLink, Conserved Domains, Links

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DEFINITION  estrogen receptor
ACCESSION   1204262A
VERSION     1204262A  GI:224957
DBSOURCE    prf: locus 1204262A;

            state: fibrosarcoma;
            taxonomy: Mammalia.
KEYWORDS    Estrogen Receptor; Human; cDNA Clone; Breast Cancer; Seq
            Determination; 6460bp; 595AAs; Expression in HeLa Cell; Binding of
            Estradiol; Seq Homol with erbA Protein; Hydropathy Plot.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 595)
  AUTHORS   Green,S., Walter,P., Kumar,V., Krust,A., Bornert,J.M., Argos,P. and
            Chambon,P.
  TITLE     Human oestrogen receptor cDNA: sequence, expression and homology to
            v-erb-A
  JOURNAL   Nature 320 (6058), 134-139 (1986)
   PUBMED   3754034
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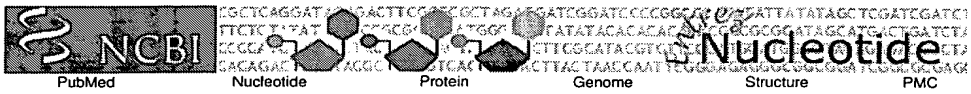

1: X51416. Reports **Human mRNA for st...[gi:36608]** Links

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ACCESSION   X51416 Y00290
VERSION     X51416.1  GI:36608
KEYWORDS    hormone receptor; receptor; steroid hormone receptor; transmembrane
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SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 2402)
  AUTHORS   Giguere,V., Yang,N., Segui,P. and Evans,R.M.
  TITLE     Identification of a new class of steroid hormone receptors
  JOURNAL   Nature 331 (6151), 91-94 (1988)
   PUBMED   3267207
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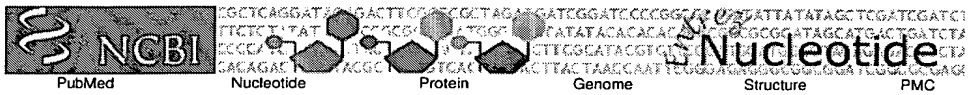

1: X03635. Reports Homo sapiens mRNA...[gi:31233] Links

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ACCESSION   X03635 M11457
VERSION     X03635.1  GI:31233
KEYWORDS    estrogen receptor; receptor; steroid hormone receptor.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
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            Hominidae; Homo.
REFERENCE   1  (bases 1 to 6450)
  AUTHORS   Green,S., Walter,P., Kumar,V., Krust,A., Bornert,J.M., Argos,P. and
            Chambon,P.
  TITLE     Human oestrogen receptor cDNA: sequence, expression and homology to
            v-erb-A
  JOURNAL   Nature 320 (6058), 134-139 (1986)
   PUBMED   3754034
COMMENT     Data kindly reviewed (28-OCT-1986) by P. Chambon.
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1: 1JAI. Reports Chain , H-Ras P2...[gi:2392390]
BLink, Conserved Domains, Links

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ACCESSION   1JAI
VERSION     1JAI  GI:2392390
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            class: Gtp-Binding;
            source: Mol_id: 1; Organism_scientific: Homo Sapiens;
            Organism_common: Human; Gene: H-Ras-1; Expression_system:
            Escherichia Coli; Expression_system_strain: Ck 600 K;
            Expression_system_vector: Ptac Ras;
            Exp. method: X-Ray Diffraction.
KEYWORDS    .
SOURCE      Homo sapiens (human)
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            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 166)
  AUTHORS   Seeburg,P.H., Colby,W.W., Capon,D.J., Goeddel,D.V. and
            Levinson,A.D.
  TITLE     Biological properties of human c-Ha-ras1 genes mutated at codon 12
  JOURNAL   Nature 312 (5989), 71-75 (1984)
   PUBMED   6092966
REFERENCE   2  (residues 1 to 166)
  AUTHORS   Pai,E.F., Krengel,U., Petsko,G.A., Goody,R.S., Kabsch,W. and
            Wittinghofer,A.
  TITLE     Refined crystal structure of the triphosphate conformation of H-ras
            p21 at 1.35 A resolution: implications for the mechanism of GTP
            hydrolysis
  JOURNAL   EMBO J. 9 (8), 2351-2359 (1990)
   PUBMED   2196171
REFERENCE   3  (residues 1 to 166)
  AUTHORS   Schweins,T., Scheffzek,K., Assheuer,R. and Wittinghofer,A.
  TITLE     The role of the metal ion in the p21ras catalysed GTP-hydrolysis:
            Mn2+ versus Mg2+
  JOURNAL   J. Mol. Biol. 266 (4), 847-856 (1997)
   PUBMED   9102473
REFERENCE   4  (residues 1 to 166)
  AUTHORS   Schweins,T., Scheffzek,K., Assheuer,R. and Wittinghofer,A.
  TITLE     Direct Submission
  JOURNAL   Submitted (15-DEC-1996)
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SOURCE      Canis familiaris (dog)
  ORGANISM  Canis familiaris
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            Canis.
REFERENCE   1  (residues 1 to 83)
  AUTHORS   Watzinger,F., Mayr,B., Haring,E. and Lion,T.
  TITLE     High sequence similarity within ras exons 1 and 2 in different
            mammalian species and phylogenetic divergence of the ras gene
            family
  JOURNAL   Mamm. Genome 9 (3), 214-219 (1998)
   PUBMED   9501305
REFERENCE   2  (residues 1 to 83)
  AUTHORS   Watzinger,F.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-JUN-1996) Children's Cancer Research Institute,
            Kinderspitalgasse 6, Vienna A-1090, Austria
REFERENCE   3  (residues 1 to 83)
  AUTHORS   Watzinger,F.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-NOV-1999) Children's Cancer Research Institute,
            Kinderspitalgasse 6, Vienna A-1090, Austria
  REMARK    Sequence update by submitter
REFERENCE   4  (residues 1 to 83)
  AUTHORS   Watzinger,F.
  TITLE     Direct Submission
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1: AAC13249. Reports ras p21 [Felis ca...[gi:3043769]

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            Mammalia; Eutheria; Laurasiatheria; Carnivora; Fissipedia; Felidae;
            Felinae; Felis.
REFERENCE   1  (residues 1 to 83)
  AUTHORS   Watzinger,F., Mayr,B., Haring,E. and Lion,T.
  TITLE     High sequence similarity within ras exons 1 and 2 in different
            mammalian species and phylogenetic divergence of the ras gene
            family
  JOURNAL   Mamm. Genome 9 (3), 214-219 (1998)
   PUBMED   9501305
REFERENCE   2  (residues 1 to 83)
  AUTHORS   Watzinger,F.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-JUN-1996) Children's Cancer Research Institute,
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ACCESSION   621P
VERSION     621P  GI:494922
DBSOURCE    pdb: molecule 621P, chain 32, release Jun 6, 1991;
            deposition: Jun 6, 1991;
            class: Oncogene Protein;
            source: Human (Homo Sapiens) Cellular Harvey-Ras Gene Truncated And
            Expressed In (Escherichia Coli);
            Exp. method: X-Ray Diffraction.
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
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            Hominidae; Homo.
REFERENCE   1  (residues 1 to 166)
  AUTHORS   Pai,E.F., Krengel,U., Petsko,G.A., Goody,R.S., Kabsch,W. and
            Wittinghofer,A.
  TITLE     Refined crystal structure of the triphosphate conformation of H-ras
            p21 at 1.35 A resolution: implications for the mechanism of GTP
            hydrolysis
  JOURNAL   EMBO J. 9 (8), 2351-2359 (1990)
   PUBMED   2196171
REFERENCE   2  (residues 1 to 166)
  AUTHORS   Krengel,U., Schlichting,L., Scherer,A., Schumann,R., Frech,M.,
            John,J., Kabsch,W., Pai,E.F. and Wittinghofer,A.
  TITLE     Three-dimensional structures of H-ras p21 mutants: molecular basis
            for their inability to function as signal switch molecules
  JOURNAL   Cell 62 (3), 539-548 (1990)
   PUBMED   2199064
REFERENCE   3  (residues 1 to 166)
  AUTHORS   Krengel,U., Scherer,A., Kabsch,W., Wittinghofer,A. and Pai,E.F.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JUN-1991)
COMMENT     Revision History:
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      121 aartvesrqa qdlarsygip yietsaktrq gvedafytlv reirqh
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Range: from begin to end Features: SNP graph CDD MGC HPRD STS tRNA Refre:
BLink, Conserved Domains, Links

1: AAB02605. Reports c-Ha-ras1 p21 pro...[gi:190891]

LOCUS AAB02605 189 aa linear PRI 13-FEB-2004
DEFINITION c-Ha-ras1 p21 protein [Homo sapiens].
ACCESSION AAB02605 CAA23837
VERSION AAB02605.1 GI:190891
DBSOURCE locus HUMRASH accession J00277.1
KEYWORDS .
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 5 (residues 1 to 189)
AUTHORS Capon,D.J., Chen,E.Y., Levinson,A.D., Seeburg,P.H. and Goeddel,D.V.
TITLE Complete nucleotide sequences of the T24 human bladder carcinoma oncogene and its normal-homologue
JOURNAL Nature 302 (5903), 33-37 (1983)
PUBMED 6298635
COMMENT On Feb 12, 2004 this sequence version replaced gi:35887.
The human genome contains a family of genes with homology to the Harvey murine sarcoma virus oncogene (c-Ha-ras). Two of these homologues are detectable by high stringency Southern hybridizations; the c-Ha-ras1 and c-Ha-ras2 genes, which occur on BamHI fragments of varying sizes from 3 to 9 kb because of allelic polymorphisms in the flanking regions.
Genomic mapping and nucleotide sequencing has shown that c-Ha-ras1 is the normal progenitor of the transforming gene found in several human tumor cell lines (T24 bladder carcinoma; EJ bladder carcinoma; Hs242 lung carcinoma; SK2 melanoma; and HS578T mammary carcinosarcoma). The only difference within the coding exons of the c-Ha-ras1 proto-oncogene and the oncogene of the T24 and EJ cell lines is a 'g' to 't' transversion within codon 12 that results in the substitution of valine for glycine at this position in the p21 protein encoded by c-Ha-ras1. The mutation responsible for transforming ability of the p21 protein in the SK2 and Hs242 cell lines is an 'a' to 't' transversion within codon 61 that results in the substitution of leucine for glutamine at this position. The mutation responsible for transforming ability of the p21 protein in the HS578T cell line is a 'g' to 'a' transition within codon 12 that results in the substitution of Aspartic acid for glycine at this position [9]. Because this 'g' to 'a' transition abolishes a MspI/HpaII site within the transformed allele, [9] was able to determine that both of the H-ras1 alleles found in normal cells from the same individual from which the HS578T cells were obtained, had the normal sequence at this position.
A region of repeated DNA consisting of the 28bp consensus sequence 'cactccccttctctccaggggacgcca' begins at position 4755. The repeat occurs 29 times in the plasmid used for this sequence but may occur more times in the native DNA. This region is known to be unessential for transforming activity [5].
[5] constructs a chimeric SV40 early promoter/human c-Ha-ras1 plasmid to demonstrate that upon transfection transforming activity is unaffected. [2],[5] and [7] discuss the extensive homology with the retroviral onc genes (v-has, v-bas, v-ha-ras). Complete source information:
Human genomic DNA [3],[1],[5]; human bladder carcinoma cell line T24 DNA [3],[2],[5],[7]; cDNA to mRNA, clones RS-3, RS-4 and RS-6 [4]; human bladder carcinoma cell line EJ DNA [1]; human lung carcinoma cell line Hs242 DNA [6]; human melanoma cell line SK2 DNA, clone lambda-SK2-T2 [8]; human mammary carcinosarcoma cell line SH578T DNA, clone lambda-HS578T [9],[10].
FEATURES Location/Qualifiers
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/db_xref="taxon:9606"

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LOCUS       MAU38462                488 bp    DNA     linear   ROD 08-NOV-1995
DEFINITION  Mesocricetus auratus Ha-ras protein (c-Ha-ras) gene, exon 1 and 2,
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ACCESSION   U38462
VERSION     U38462.1  GI:1053060
KEYWORDS
SOURCE      Mesocricetus auratus (golden hamster)
  ORGANISM  Mesocricetus auratus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Cricetidae; Cricetinae; Mesocricetus.
REFERENCE   1  (bases 1 to 488)
  AUTHORS   Chakravarti,D., Cavalieri,E.L. and Rogan,E.G.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-OCT-1995) Dhrubajyoti Chakravarti, Eppley Institute,
            University of Nebraska Medical Center, 600 South 42nd Street,
            Omaha, NE 68198-6805, USA
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1: 1WQ1G Reports BLink, Conserved Domains, Links
Chain G, Ras-Rasgap Complex
gi|3402130|pdb|1WQ1|G[3402130]

2: 1WQ1R Reports BLink, Conserved Domains, Links
Chain R, Ras-Rasgap Complex
gi|3402129|pdb|1WQ1|R[3402129]

3: 1A2B Reports BLink, Conserved Domains, Links
Chain , Human Rhoa Complexed With Gtp Analogue
gi|3318980|pdb|1A2B| [3318980]

4: 2RGF Reports BLink, Conserved Domains, Links
Chain , Rbd Of Ral Guanosine-Nucleotide Exchange Factor (Protein), Nmr, 10 Structures
gi|2982004|pdb|2RGF| [2982004]

5: 1JAI Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant G12p, Complexed With Guanosine-5'-[beta,Gamma-Methylene] Triphosphate And Manganese
gi|2392390|pdb|1JAI| [2392390]

6: 1JAH Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant G12p, Complexed With Guanosine-5'-[beta,Gamma-Methylene] Triphosphate And Magnesium
gi|2392389|pdb|1JAH| [2392389]

7: BAA20127 Reports BLink, Conserved Domains, Links
Rap 1B [Rattus norvegicus]
gi|2116982|dbj|BAA20127.1|[2116982]

8: BAA20126 Reports BLink, Conserved Domains, Links
Rap 1A [Rattus norvegicus]
gi|2116980|dbj|BAA20126.1|[2116980]

9: AAC52724 Reports BLink, Conserved Domains, Links
RalGDS-like factor
gi|1354501|gb|AAC52724.1|[1354501]

10: 1AGP Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein Mutant With Gly 12 Replaced By Asp

(G12d) Complexed With Guanosine-5'-[b,G-Imido] Triphosphate
gi|515076|pdb|1AGP| [515076]

11: 1GNP Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein Complexed With 3'-O-(N-Methyl-Anthraniloyl-2'-Deoxyguanosine-5'-[beta,Gamma-Imido]- Triphosphate (Residues 1 - 166)
gi|1127267|pdb|1GNP| [1127267]

12: 1PLL Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein Mutant With Gly 12 Replaced By Pro (G12p) Complexed With Guanosine-Diphosphate
gi|576244|pdb|1PLL| [576244]

13: 1PLK Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein Mutant With Gly 12 Replaced By Pro (G12p) Complexed With Guanosine-Triphosphate
gi|576243|pdb|1PLK| [576243]

14: 1PLJ Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein Mutant With Gly 12 Replaced By Pro (G12p) Complexed With P3-1-(2-Nitrophenyl)ethyl-Guanosine-5'-(B,G-Imido)-Triphosphate
gi|576242|pdb|1PLJ| [576242]

15: 821P Reports BLink, Conserved Domains, Links
Chain , C-H-Ras P21 Protein (Residues 1 - 166) Mutant With Gly 12 Replaced By Pro (G12p) Complex With Guanosine-5'-[b,G-Imido] Triphosphate
gi|494936|pdb|821P| [494936]

16: 721P Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant With Gln 61 Replaced By Leu (Q61l) Complex With Guanosine-5'-[b,G-Imido] Triphosphate
gi|494925|pdb|721P| [494925]

17: 621P Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant With Gln 61 Replaced By His (Q61h) Complex With Guanosine-5'-[b,G-Imido] Triphosphate
gi|494922|pdb|621P| [494922]

18: 521P Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant With Gly 12 Replaced By Val (G12v) Complex With Guanosine Triphosphate
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19: 421P Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant With Gly 12 Replaced By Arg (G12r) Complex With Guanosine-5'-[b,G-Imido] Triphosphate
gi|494886|pdb|421P| [494886]

20: 221P Reports BLink, Conserved Domains, Links
Chain , H-Ras P21 Protein Mutant With Asp 38 Replaced By Glu (D38e) Complex With Guanosine-5'-[b,G-Imido] Triphosphate
gi|494721|pdb|221P| [494721]

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